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Evolution

How much worse can variants get?

The coronavirus could turn into just another cold, but it could also evolve into something much deadlier, reports **Michael Le Page**

THE devastating impact of the new coronavirus variants is becoming clear. The more transmissible B.1.1.7 variant first identified in the UK is causing a surge of infections and deaths around the world. Is this just the beginning? Could even nastier variants evolve?

When considering future variants, there are three main properties to worry about: transmissibility, evasion of immunity to past infection or vaccines, and lethality. Of these, transmissibility is the most important. The new coronavirus, SARS-CoV-2, is far less lethal than the Ebola virus, but it has killed far more people because it is much better at spreading.

We still don't understand why the B.1.1.7 variant is at least 50 per cent more transmissible than other variants, says Joe Grove at University College London. But his work suggests that the spike proteins on its surface are a bit better than those of other variants at getting into human cells.

The bad news is that he has found that the spike protein of a coronavirus isolated from pangolins is around 100 times better at getting into human cells, suggesting there is plenty of scope for SARS-CoV-2 to evolve to become even more transmissible. "Until recently, SARS-CoV-2 was not living

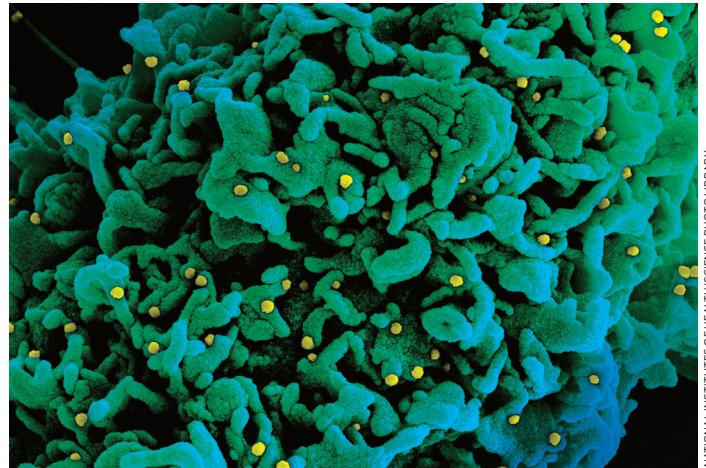
experiments as he wanted to avoid any risk of escape.

Then there is immune evasion. Our immune system protects us in two main ways. It produces T-cells that detect and destroy infected cells before the virus can replicate, and antibodies that bind to the virus to stop it infecting cells.

The most effective antibodies, called neutralising antibodies, bind to the part of the spike protein that helps the virus get into cells. That means mutations in this region can allow the virus to evade antibodies to some extent, which is what happened in the B.1.351 variant first spotted in South Africa and the P.1 variant that was first seen in Brazil (see page 7).

But there are limits on further evolution. "The spike protein is a machine with moving parts that have important roles," says Grove. If mutations arise that break the machine, the virus cannot infect cells.

It is also much harder for the virus to evade the T-cell response because this remains effective as long as T-cells recognise any part



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A human cell infected with the B.1.1.7 variant of coronavirus

of the virus. For this reason, T-cell resistance is expected to evolve much more slowly than antibody resistance, giving us time to tweak vaccines if necessary. "It appears to be difficult for the virus to completely escape T-cells," says Andreas Berghthaler at the Research Center for Molecular Medicine in Austria.

Next is lethality. There is growing evidence that B.1.1.7 is slightly more lethal than older variants. "There's a reasonable possibility it could even get worse," says Aris Katzourakis at the University of Oxford.

While it is often said that viruses evolve to become less deadly, there is no reason to think this will be the case with SARS-CoV-2, says Katzourakis. "It can easily be transmitted before it kills its hosts, so there's not much selective pressure for this virus to become less virulent," he says.

The good news is that the vaccines work even better than hoped and that the coronavirus is unlikely to be able to completely evade vaccine protection any time soon. As more people acquire immunity, many experts still believe that the virus could turn into just another cold virus, like the existing human coronaviruses.

But with most people on the planet yet to be vaccinated, we are a long way from that point and the vaccines may require tweaking more than once to remain effective. "This game of evolutionary to and fro with the virus is going to go a few more rounds yet," says Grove. ■

"A coronavirus in pangolins is about 100 times better at entering our cells than the one causing covid-19"

in humans," he says. "Now it is undergoing optimisation for humans and there is no reason to assume it is going to stop here."

But Grove stresses that we can't be sure the spike protein changes are behind the higher transmissibility, not least because he didn't use live viruses in his

The covid-19 risk from our pets

In humans, the new coronavirus appears to be changing relatively slowly, but it seems to mutate much faster in animals.

When Sue VandeWoude's team at Colorado State University infected dogs, cats and hamsters with the virus, many mutations arose within days. This could be a source of dangerous variants if they jumped back into people.

"There's a risk, albeit a very low risk, of the virus becoming more virulent or transmissible," says VandeWoude.

While many dogs and cats have

been infected by humans – cats are particularly susceptible – there is no evidence of pets infecting people. However, the virus has jumped to mink and then back to people. So far, this hasn't given rise to more dangerous variants.

Another worrying finding is that the B.1.1.7 variant infects lab mice, unlike older variants. If this variant circulates in wild mice, it could infect cats and then people.

As a result, VandeWoude thinks we should consider vaccinating cats against the virus.